THE ATOMIC PROCESSES OF DISEASE*

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LIFE in the human body is dependent upon chemical processes, but vital activities cannot be considered to be governed by the rules of a simple chemical system. There exist factors which modify these chemical processes so that stochiometric (or purely chemical) explanations are not completely satisfying unless qualified. In vital activities, the processes are based upon colloid structure, and life may be defined as a continuance of chemical reactions in a colloid medium. For this reason, surface action is of greatest importance and the reactions of colloids, dependent upon the degree of dispersity, go far to explain the processes of the colloid protoplasm.

Mechanism is, therefore, as important as chemical reaction. Protoplasm, which is the basis of life, is a colloid, and the unit of protoplasm is the cell. The cell is an acid (or less alkaline, p.H. 6.2—6.8) colloid particle, surrounded and contained by a semi-permeable cell membrane, and exists in an alkaline medium (the blood plasma, p.H. 7.40). This arrangement is ideal for bio-electric variation and potential differences across a surface, for the acid cell with its membrane, acts as an electrode reversible to cations. For this reason, surface action is of greatest importance, and Bayliss[1] teaches that enzymes in the human body obey the usual laws of catalytic phenomena, particularly in heterogeneous systems in which the reactions take place at the surfaces of the colloids, and that the reactions are reversible, the equilibrium point being determined by the effective concentration of water. In muscular contraction, for another example, Bernstein[2] has given definite evidence to show that the energy of contraction is surface energy, and that the muscles suffer thermal changes peculiar to surface energy. Many other vital phenomena can be explained upon the same basis.

The functioning cells of the body are controlled and regulated by impulses generated by the cells of other organs, and conducted to and fro by structures specially evolved for this purpose. This is nerve action, and there are in the human body two nervous systems—the conscious or cerebral system and the vegetative or unconscious system (also called sympathetic, involuntary or autonomic). The cerebral system has to do with voluntary control (or willed activity) and the vegetative system has to do with involuntary action or the unconscious organic processes. The vegetative nervous system controls the heart that beats, the stomach and intestines that move and digest, the kidneys that secrete, and all the varied processes of our unconscious life and without our control. This vegetative system consists of two opposed and balanced parts, the vagus and sympathetic divisions. (The vagus part is also called para-sympathetic). The control by the vegetative nervous system is largely effected through its action upon smooth, involuntary, or non-striated muscle in contra-distinction to striated or voluntary muscle which is controlled by the cerebral or conscious system. Smooth, involuntary, or non-striated muscle is very widely distributed in the body, in the pupil, in the heart, blood vessels and capillaries (Rouget cells), in the great organs, stomach, intestine, spleen, etc. The vagus division, for example, makes the heart beat slower and the sympathetic division makes the heart beat faster. The vagus makes the stomach and intestines contract, and the sympathetic makes the stomach and intestines dilate, etc.

In the mechanism of human life and its deviations in disease, there must be considered:—(1) *the application of energy from atoms*, (2) *the colloid character of the protoplasm of the human body* and (3) *the control exercised over these processes by the vegetative nervous system.*

The colloids of the human body are amphoteric (neutral or without potential) until vitalized by electrolytes which give them charge. It is for this reason that the inorganic salts, although comprising only about two per cent of the body weight, are of supreme importance. These determine the potential, so that the relatively acid cell with its semi-permeable membrane, existing in an alkaline medium, is dependent upon external conditions for the various manifestations of life.

*Abstract of paper read by title at Canadian Medical Association, Regina, June, 1925.

Energy production is dependent in these cells upon organization or mechanism and potential differences across a membrane or surface. The energy is the energy of electrons and dependent, as are the properties of elements upon the configuration of electrons, particularly those in the outer layer. Langmuir[3] has shown that it is possible to predict the properties of elements according to the configuration of electrons, and that the tendency to give or take electrons is dependent upon the presence of electro-positive or electro-negative elements, capable of taking or giving electrons. Naturally, our knowledge of these forces is at present limited, but, when in the future, we are able to calculate the force between the electrons and the positive nuclei of the atoms it will be possible to account for all phenomena, physical and chemical, physiological and pathological, by calculating the forces between molecules, electrons and atoms. If these forces are all electrical in their nature, the force holding them together in a chemical compound like NaCL, and the force, binding hæmoglobin, or producing consolidation in pneumonia, are of the same nature, and dependent upon the relation of the electrons to the positive nucleus. Univalent substances, like Na and K, with one outer electron, have an action more like each other in the human body, and antagonistic to bivalent elements, like Ca and Mg, with two electrons in their outer ring.

The cells of the human body act like negative suspensoids, reversible to cations, controlled by the buffer salts, and their potential differences are due to traces of electrolytes, exactly as has been shown by Murkerjee[4] in colloid experiments on negative suspensoids. Murkerjee has also shown that elements have greater or less adsorbability to negative suspensoids in the order, Th> Al> Ba> Sr> Ca> Mg> H> Cs> Rb> K> Na> Li>, and in the human body, the same order, Ca> Mg> K> Na>, Li, holds for the production of acidity, reduction of blood pressure and other effects. The Ca and Mg salts produce acid conditions in the blood (plasma p.H.), urine, stool and other secretions, and the Na and K salts produce alkaline conditions. The Ca and Mg salts stimulate the vagus side of the vegetative nervous system, and the Na and K salts stimulate the sympathetic part. Murkerjee[5] has, indeed, suggested in a recent paper that the results obtained by the biologists upon unicellular organisms are due to this action, and that "at least one of the main causes which is responsible for the ionic antagonism as observed by Lillie, Osterhout, Loeb and Clowes is the effect of the ions on the electrical charge of the dispersed system."

Protoplasmic or vital action may then be crudely represented by the following diagram:—

Nucleus, electron	cation, anion	electrolyte, water	Protoplasmic action or
nucleus, electron	colloid, film	colloid cell, cell membrane	vital processes

However, in the human body, control of processes by nerve action is of importance. The smooth muscle of the human body may be taken as an index of the balance of the vegetative nervous system, and, as the pupil of the eye dilates with sympathetic action and contracts with vagus action, so the greatest mass of smooth muscle in the body, the stomach and intestines, is similarly influenced. It has been found possible by Ludlum and myself[6], by means of x-ray pictures and fluoroscopic examinations of the gastrointestinal tract, to determine the balance of the vegetative nervous system, upon the basis of postural tone and haustral arrangement. We also found that when the blood plasma was more acid (lowered p.H.), there was a tendency to vagus effects and, when the blood plasma was more alkaline, (higher p.H.), there was a tendency to sympathetic effects. These were not only shown in the smooth muscle of the intestine, but upon the heart (blood pressure and pulse rate) and smooth muscle elsewhere. Here, then, was a relation between chemical action and body processes, so that to quote Crozier, the biologist: "typical vital processes obey quantitatively the laws of ordinary chemical dynamics."

The nervous control over the functioning cells of the body is exercised mainly through the vegetative system, which has a double innervation of stimulation and inhibition to smooth muscle and to every organ of the body. This nervous system controls and expends daily three quarters of the total human energy in processes without control of the will. The steady maintenance of the machinery of life is controlled by processes of which we are unconscious. The vegetative nervous system controls circulation, digestion, metabolism and elimination without aid from the cerebro-spinal or conscious nervous system. "Who, by taking thought, can add a cubit to his stature," and who, by taking thought, can increase his growth, make his kidneys secrete better, or alter his metabolism? This is controlled by a nervous system which is a law unto itself and king within its own realm. The vegeta-

tive nervous system has among its functions the control of the smooth muscle of the body; when the large extent of this smooth muscle and its distribution in the important organs of the body are considered, the great influence of this form of control may be appreciated. The control of the area of the blood vessel capillaries alone (which in a small man amount in area to 120,000 square yards) shows the importance of this unconscious influence, and control of the capillaries is only one function of the vegetative nervous system.

From the influence upon the smooth muscle of the gastro-intestinal tract, it has been found possible by the fluoroscope and x-ray pictures of the postural tone and haustral arrangement to estimate the balance of the two branches (the vagus-sympathetic) of the vegetative nervous system. This balance in health showed a regularity of arrangement of contraction and dilation of the gastro-intestinal tract, particularly in the large intestine where the vagus contracts and the sympathetic dilates the amplitude. The postural arrangement of haustra of the large intestine may be taken, in the absence of drugs and purgatives and under specified conditions, as an index of the vagus-sympathetic balance of the vegetative nervous system. This statement has been checked by many hundred x-ray pictures and by other workers.

In the study of the vagus-sympathetic balance, when there was vagus preponderance, it was found that the hydrogen ion concentration of the blood was increased (p.H. decreased, upon the acid side of the normal p.H.=7.40): and when there was sympathetic preponderance, the hydrogen ion concentration of the blood was decreased (p.H. higher, more alkaline than p.H.=7.40). This alteration in the postural tone and haustral arrangement, as an index of the vagus-sympathetic balance, was greater and greater the more the hydrogen ion concentration of the blood plasma deviated from normal, so that it was possible to create a scale of x-ray pictures (Figs. 2-10) of the colon corresponding to specified hydrogen ion concentration. The more vagus preponderance, the greater was the contraction of the smooth muscle of the large intestine and the higher the hydrogen ion concentration. (It will be noted that Sorensen's method of measuring the hydrogen ion concentration makes the nomenclature a little obscure. When the hydrogen ion concentration is higher, the p.H.—Sorensen's figure—is lower and *vice versa*). When the postural tone was less contracted than normal and there was sympathetic preponderance, the hydrogen ion concentration was less (p.H. higher). This rule held generally and in the main with certain very definite exceptions. At menstruation, the ratio was frequently upset for two or three days, but finally would correlate itself again. In a few other cases it failed to correlate, but usually was explained by drug medication (particularly such as veronal, allonal, luminal, etc.). It reacted according to rule after the drugs were removed. Some cases, however, only correlated occasionally and could not be explained. To expect that the correlation would be exactly interpreted is expecting too much, but a correlation table, taken for us by Thurstone, Assistant Professor of Psychology at the University of Chicago, showed that it is possible for the trained observer to translate the smooth muscle posture of the stomach and large intestine into terms of the hydrogen ion concentration of the blood plasma with a very small margin or error.

The vagus-sympathetic balance shows itself not only in the size of the large intestine, but in the rate of change in haustral pattern and in regularity of haustration, an evidence of nerve integration. For example, in morphine, a vagus stimulant which contracts smooth muscle (well seen in the contracted pupil), sympathetic influence is cut down and there is vagus preponderance, the difference in size of the intestine may be hard to judge, but the free sacral innervation (pelvic vagus) shows itself mainly in rapidity of haustral change and choreic irregularity patterns. But generally and in the main, the postural tone is sufficient expression of the vagus-sympathetic balance.

In acid (less alkaline) states of the blood plasma, then, the vagus side of the vegetative nervous system is preponderant, and in alkaline states, the sympathetic side is preponderant. After all, this is only what is to be expected from the experiments of Daly and Clark[7] and Drury[8] Cowles[9] upon the mammalian heart. In acid (acid side of p.H.=7.40) states of the perfused heart, the rate of the auricle fell and the vagus inhibited the heart; and in alkaline states, the rate increased and the sympathetic stimulated the heart. So that in the intestine, where the vagus stimulates contraction, acid states are vagus preponderance, the opposite from that of the heart.

Here, then, is the striking fact that acid (or less alkaline) conditions of the blood plasma predispos teo vagus preponderance and alkaline states predispose to sympathetic preponderance with

the far reaching influence of the vegetative nervous system upon all organs, (circulation and metabolism) in these different states. Nerve action can so be connected quantitatively with chemical processes. Our experiments with the various cations, ingested and injected into the human body, showed that the vagus part of the vegetative nervous system was made preponderant by the bi- and tri-valent cations and anions; and the sympathetic part of the vegetative nervous system was made preponderant by the univalent cations like sodium and potassium. This was checked both by the postural tone (smooth muscle reaction) of the colon and the p.H. of the blood. In addition, many experiments by others upon acid-base conditions can be translated in terms of vegetative nervous preponderance. (For example, the experiments of Haldane[10] *et al*, Gamble, Hamilton and Blackfan[12], [13], [14], and Salvesen[11] *et al* in the production of acidosis by calcium and magnesium.)

The conclusion is, therefore, reached that the balance of the vegetative nervous system, as shown in the smooth muscle of the intestine, acts and reacts like the colloid in the chemical experiment, or like the biological experiments upon the single-celled organism in regard to the cations. The univalent cations, Na and K, which increase sympathetic action, increase permeability, conductivity and dispersion of the colloid and act in an entirely different direction to the bi- and trivalent cations, like Ca and Mg, which decrease permeability, conductivity and cause coalescence of the colloid and increase vagus action. The expression of the vegetative nervous system corresponds to the influence of these elements to the action of similar crystalloids upon colloids in biological experiments; so that the inference may be drawn, in certain states of vagus-sympathetic balance, as to the condition of the body cell in general as to permeability, conductivity, dispersion, etc. In sympathetic preponderance, there is increased cell permeability and conductivity and dispersion; in vagus preponderance, there is decreased cell permeability, conductivity and coalescence. It is possible in this way to explain disease and symptoms of disease in terms of cell changes and to supply a scientific working hypothesis based upon the atomic theory for disease processes and medication.

The method consists in the estimation of the vagus-sympathetic balance by the smooth muscle index by means of x-rays of the gastro-intestinal tract and the measurement of the hydrogen ion concentration of the blood by the most approved methods. An index of the patient's metabolic condition can be obtained as in no other way; symptoms are translated in terms of the vegetative nervous system which, in turn, is translated into colloid cell change.

We have found that certain diseases, like tetany, etc., arranged themselves upon one or other side of the vegetative nerve balance, so that it has been possible to represent them in the following schema: See Fig. 1.

Cause	*Mechanism*	*Expression*
Energy from orientation and configuration of electrons in atoms in atoms and molecules	Coalescence of colloid Bi and tri-valent cations and anions produce vagus effects Less cell conductivity Less potential difference Anodal Negative Increased smooth muscle reaction	
INORGANIC SALTS	Lower pH (higher H-ion concentration in blood)	Most infections Colitis
	Less permeable cell membrane	Typhoid
	Vagus	Diabetes
	Plasma less alkaline	Neurasthenia
LIPOID SOLVENTS	Oxidation	
METABOLISM———	———————————	———*HEALTH*
HYDROGEN ION CONCENTRATION	Reduction Plasma more alkaline Sympathetic	Psychiasthenia
	More permeable cell membrane	Deficiency Disorders
	Higher pH (lower H-ion concentration in blood)	Tetany Rickets
OXIDATION-REDUCTION POISE	Decreased smooth muscle reaction	Syphilis
	Positive	Eclampsia
	Cathodal	Respiratory infections (Tuberculosis)
	Greater potential difference	(Pneumonia)
	Greater cell conductivity	Gastric Ulcer
	Univalent cations produce sympathetic effect	Essential Hypertension
	Dispersion of colloid	Œdema

FIG. 1

It has been possible, therefore, to translate manifestations of disease in terms of vagus-sympathetic balance and, with the aid of hydrogen ion concentration estimations of the blood plasma, in terms of chemical processes.

Disease may, therefore, be divided into two great classes: (1) *The vagus preponderant* and (2) *the sympathetic preponderant.* In the vagus preponderant, there are symptoms associated with excess of bi- and trivalent cations and anions, increased hydrogen ion concentration and increased smooth muscle reaction. With these changes must come a decrease of permeability and conductivity in the cell, increased tendency toward coalescence, or condensation of the colloid, acidity and oxidation (electron-taking) effects. In the sympathetic preponderant diseases, there are symptoms associated with excess of univalent cations (or diminution of the bi- and trivalent cations) decreased hydrogen ion concentration and decreased smooth muscle reaction. With these changes must come an increase of permeability and conductivity in the cell, increased tendency toward dispersion of the colloid, alkalinity and reduction, (electron-giving) effects.

This theory has been applied in treatment to various diseases, as gastric ulcer, etc. An example is in essential hypertension, or high blood pressure, which is controlled by the sympathetic part, and is benefited by the sodium-free diet and by the taking of calcium and magnesium salts. (Abstract sodium—add calcium and magnesium). The symptoms of disease may be explained upon the basis of this theory.

Blood pressure is a significant and fundamental process in the human body and its control is dependent upon the vegetative nervous system of which sympathetic stimulation increases and vagus preponderance decreases the blood pressure. Hypertension is a sympathetic phenomenon and all substances which reduce blood pressure are vagus stimulants, such as the calcium and magnesium salts and parathyroid extracts. In the rabbit's heart, Drury and Cowles[16] have found that there was increased rate and conduction (sympathetic effect) with a p.H. = 7.8 (alkaline side), while at p.H. = 7.0 (acid side), there was a slowed rate of the heart. This correlation of the heart action and chemical conditions bears out Crozier's statement that "chemical conditions control the activity of the central nervous tissues" and that these include control of the vegetative nervous system which governs metabolism and body processes. Not only does the degree of hydrogen ion concentration have an influence, but also the special effects of the various salts.

In the study of blood pressure, as a prominent and fundamental manifestation, it is found that the action may be represented in parallel columns. (See blood pressure effects).

Other symptoms of disease may be explained in a similar fashion. Gastric secretion, which is a function of gastric motility, is increased by vagus-effect-producing substances and decreased by sympathetic-effect-producing substances. Temperature, which is a function of water content, depends upon the imbibition of the colloid water and structural changes of colloid. Respiration is very definitely controlled by hydrogen ion concentration and oxidation-reduction poise.

The processes of disease are but deviation from normal protoplasmic processes and these depend upon colloid reactions in an aqueous medium, so must obey the laws of colloid chemistry. In this, the most important principles are surface action, adsorption and disorption, the electrical double layer of Helmholtz, and the effect of the electrical charge of ions. In this must be considered the control of the vegetative nervous system and dis-

BLOOD PRESSURE EFFECTS

Substances which Decrease Blood Pressure	*Substances which Increase Blood Pressure*
Are Vagus Stimulants:	Are Sympathetic Stimulants:
Make urine acid:	Make urine alkaline:
Make blood plasma less alkaline:	Make blood plasma more alkaline:
Bi- and trivalent cations and anions, like Ca, Mg and HCL	Univalent cations like Na and K
Decrease permeability of cell in biological experiments:	Increase permeability of cell
Decrease conductivity	Increase conductivity
Oxidant (takes electrons):	Reductants (give electrons):
Cause greater adsorbability to negatively charged surfaces	Cause less adsorbability to negatively charged surfaces:
Make water-in-oil emulsions:	Make oil-in-water emulsions (Clowes)[18]
Cause solidification of the protoplasm when injected within the cell:	Cause liquefaction of the protoplasm when injected within the cell. (Chambers)[19].

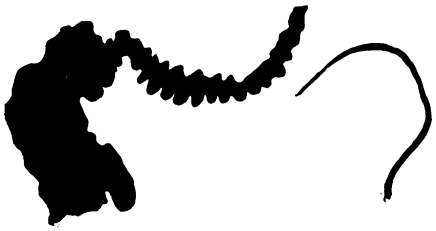

FIG. 2.—Colon with pH of 7.2 in the blood.

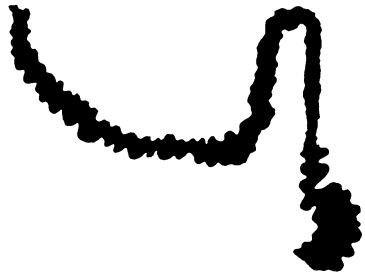

FIG. 3.—Colon with pH of 7.34 in the blood.

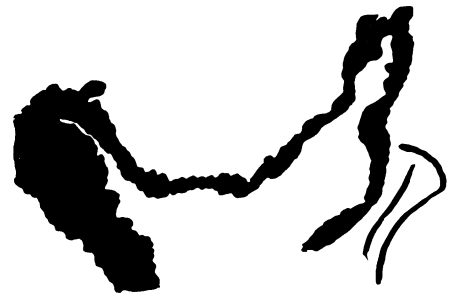

FIG. 4.—Colon with pH of 7.35 in the blood.

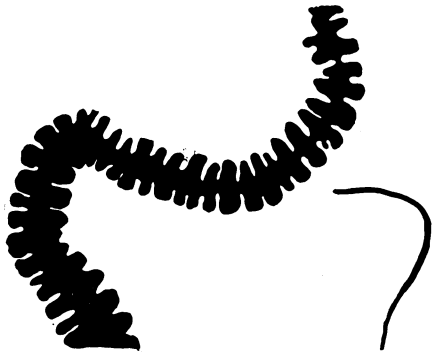

FIG. 5.—Colon with pH 7.4 in the blood.

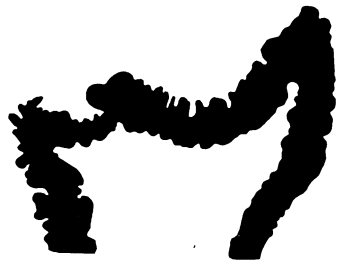

FIG. 6.—Colon with pH of 7.45 in the blood.

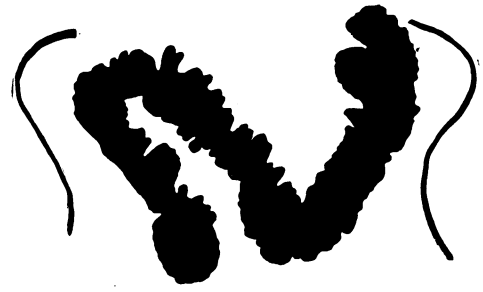

FIG. 7.—Colon with pH of 7.5 in the blood.

FIG. 8.—Colon with pH of 7.6 in the blood.

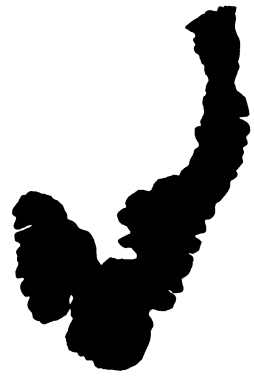

FIG. 9.—Colon with pH of 7.7 in the blood.

FIG. 10.—Colon with pH of 7.8 in the blood.

case can be divided into two great classes: (1) The vagus preponderant and (2) the sympathetic preponderant. These classes correspond to alteration in the colloid upon one or other side of the normal bio-electric variation or charge. In classification, the hydrogen ion concentration of the blood and the smooth muscle reaction is of great importance.

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